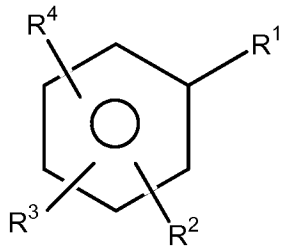
6,416,779) or D'Augustine et al. in view of Robbins et al. and Lambert.

Claim 1 is directed to an exoprotein inhibitor for inhibiting the production of exoproteins from Gram positive bacteria in and around a vagina. The exoprotein inhibitor comprises a non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. The non-absorbent substrate has deposited thereon an effective amount of a first active ingredient having the general formula:



wherein R^1 is $-OR^6OH$; R^6 is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^2, R^3, and R^4 are independently selected from the group consisting of H, OH, COOH, and $-C(O)R^9$; R^9 is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety, wherein the first active ingredient is effective in inhibiting the production of exoprotein from Gram positive bacteria.

Robbins et al. disclose an analysis of the influence of 17 commercially available tampons on the production of toxic shock syndrome toxin 1 (TSST-1) by *S. aureus* using a tampon disk method. Specifically, a disk containing 10-ml of agar medium

was overlaid with a Gelman GN-6 0.45-µm filter membrane and spread inoculated with 0.05 ml of an overnight still culture of *S. aureus* FRI-1169. In some samples, 10% blood was added to the agar medium. The test tampon was laid on the membrane and gently pressed down for uniform contact with the inoculated membrane. The disk was then sealed and incubated at 37°C for 19 hours. A plate count agar was used for enumeration of colonies in the tampon and membrane and a single gel diffusion tube method was used to determine the toxin content of the agar layer under the tampon and membrane. It was found that the amount of toxin produced increased with all tampons when blood was added to the agar medium, with an average of 42% over that without the addition of blood. Robbins et al. teach that the important functions of tampons may be to support the vaginal infection by supplying a fibrous surface for heavy colonization and to provide a sufficiently aerobic environment for toxin production.

Robbins et al. further disclose the effect of Aqualon, one surfactant, and one deodorant used in tampon manufacturing on the growth and TSST-1 production by the *S. aureus*. It was found that while the Aqualon and deodorant had little to no effect, the presence of the surfactant resulted in a decrease in CFU recovered from the disk with a corresponding decrease in TSST-1 production associated with the disk.

Lambert discloses a method of examining the effect of inoculum size on the degree of inhibition observed with respect to inhibitor concentration. Specifically, the inoculum size dependencies of phenethyl alcohol, phenoxyethanol, *p*-chloro-*m*-cresol, trichloro-phenol, thymol, and dodecyltrimethylammonium bromide against *S. aureus* were analyzed. For all inhibitors

examined, it was found that at lower inoculum levels, there was a greater biocidal effect, whereas at higher inoculum levels, there was a greater degree of quenching of the biocide, causing the inhibitor to act more as a simple (sublethal) inhibitor. As such, the method developed in Lambert may be used to quantify the effect in the region between reversible and irreversible damage, or sublethal injury to cell death. Furthermore, it was found in Lambert that phenethyl alcohol is a better inhibitor than phenoxyethanol against *S. aureus*.

Both Robbins et al. and Lambert fail to disclose the use of phenoxyethanol (or any compound having the structure of the first active ingredient as required in claim 1) on a non-absorbent substrate for insertion into the vagina for inhibiting exoproteins from Gram positive bacteria. Additionally, no where in Robbins et al. or Lambert is a non-absorbent substrate being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche even mentioned. In an attempt to find each and every element of claim 1 as required by the M.P.E.P. for a determination of *prima facie* obviousness, the Office cites the D'Augustine et al. reference for combination with Robbins et al. and Lambert.

D' Augustine et al. disclose devices, methods, and compositions for treating vaginal fungal, bacterial, viral, and parasitic infections by intravaginal or transvaginal administration of therapeutic and/or palliative antifungal, antibacterial, antiviral or parasiticidal drugs to the vagina or to the uterus. Specifically, a device such as a tampon, tampon-like device, vaginal ring, pessary, cervical cup, vaginal

sponge, intravaginal tablet, or intravaginal suppository, delivers the drug, which can be in the form of a paste, cream, ointment, microcapsule, solution, powder, or gel having a sufficient thickness to maintain prolonged vaginal epithelium and mucosa contact. In one embodiment, the drug can be incorporated into a cream, lotion, foam, paste, ointment, or gel which can be applied to the vagina using an applicator.[1]

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. §2143 requires that the Office must meet three criteria: (1) the prior art references must teach or suggest all of the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references, and (3) there must be some reasonable expectation of success. An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of the case. The common sense of those skilled in the art can demonstrate why some combinations would have been obvious where others would not. The Office has clearly failed to meet its burden under number (2) above, as there is no motivation or suggestion to combine the Robbins et al., Lambert, and D' Augustine et al. references, and further, a close reading of the cited references actually teaches away from the combination, to arrive at Applicants' claim 1. It simply would not have been obvious to one skilled in the art to arrive at Applicants' claimed combinations.

Specifically, as noted above, neither Robbins et al. nor

[1] D' Augustine et al. at column 18, lines 24-26.

Lambert teach the use of phenoxyethanol on a non-absorbent substrate for inhibiting exoprotein production. At best, Robbins et al. teach that the use of a surfactant during the manufacturing of a tampon may inhibit exoprotein production and growth of *S. aureus*. No where, however, is phenoxyethanol even mentioned. Furthermore, while Lambert does analyze phenoxyethanol as one of six inhibitors that may inhibit exoprotein production, Lambert expressly states that phenethyl alcohol is a better inhibitor as compared to phenoxyethanol. As such, why would one skilled in the art, reading Robbins et al. and/or Lambert, choose phenoxyethanol as an inhibitor of exoprotein production from Gram positive bacteria? As Lambert actually teaches away from using phenoxyethanol, one skilled in the art simply would not and could not. Specifically, at best, one skilled in the art reading Robbins et al. and/or Lambert would look to using a surfactant and/or phenethyl alcohol as possible inhibitors of exoprotein production.

The D'Augustine et al. reference fails to overcome the above shortcomings. As noted above, D'Augustine et al. teach numerous antibacterial compositions for treating bacterial infections of the vagina. As such, why would one skilled in the art pick phenoxyethanol over all of the other non-toxic, antibacterial compositions present in the art, particularly when D'Augustine et al. provide numerous suitable antibacterial compositions to use with their non-absorbent devices and do not point to any need for alternatives? D' Augustine et al. simply teach compositions that can be used as antibacterials to treat bacterial infections of the vagina and devices for delivering the compositions; and even provide several commercially

acceptable antibacterial compositions. The D' Augustine et al. reference fails to provide a reason why one skilled in the art would choose another antibacterial over those listed in the D' Augustine et al. reference or disclosed elsewhere in the art. Moreover, if one was to choose an additional antibacterial composition to use with the non-absorbent devices of D'Augustine et al., why would one choose phenoxyethanol when Lambert specifically stated that phenethyl alcohol is a better inhibitor.

Moreover, the common sense of one ordinarily skilled in the art would not have provided a reason to combine the cited reference to arrive at Applicant's exoprotein inhibitor comprising a first active ingredient having the structure as required in claim 1 deposited on a non-absorbent substrate. Specifically, as recognized by the Supreme Court in KSR International Co. v. Teleflex, Inc., "while an obviousness determination is not a rigid formula, the TSM (teaching, suggestion, motivation) test captures a helpful insight: A patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the art. Although common sense directs caution as to a patent application claiming as innovation the combination of two known [elements] according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the art to [modify] the elements as the new invention does."[2] More particularly, a court must ask whether the improvement is more than the predictable use of prior-art

elements according to their established functions. If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, §103 likely bars its patentability. For example, in KSR, the patented invention was directed towards an improved adjustable vehicle pedal assembly, and, as has long been held in the Federal Circuit, mechanical arts are predictable.[3] Recognizing that mechanical devices such as adjustable vehicle pedals and sensors can be predictably modified and combined by one skilled in the art, the Court invalidated the patent as obvious.[4]

By contrast, areas of chemistry, such as in the instant case of Applicant's exoprotein inhibitors, have been held inherently unpredictable. Specifically, as stated in In re Marzocchi,[5] "in the field of chemistry generally, there may be times when the well-known *unpredictability* (emphasis added) of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of [generalized] broad statements." That is, chemical reactions are, by their nature, unpredictable and, as such, generalized or broadly disclosed elements cannot necessarily be predictably modified.

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[2] KSR Int'l Co. v. Teleflex, Inc., et al. 550 US____, 2007 WL 1237837 at 5 (2007).

[3] *See* MPEP §2164.03 (*citing* In re Vickers, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); In re Cook, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971)); *See also,* In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991).

[4] KSR Int'l Co. v. Teleflex, Inc., et al. 550 US____, 2007 WL 1237837 at 17 (2007). Specifically, the Court held that there was convincing evidence that mounting a modular sensor on a fixed pivot point of a pedal was a design step well within the foreseeable grasp of a person or ordinary skill in the relevant art and, as such, the claimed adjustable pedal assembly of claim 4 was obvious.

[5] 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971).

As there is no motivation or suggestion to combine the Robbins et al., Lambert, and D' Augustine et al. references to arrive at each and every limitation of claim 1, claim 1 is patentable over Robbins et al. and Lambert in view of D'Augustine et al.

Claims 2-4 and 6-9 depend directly or indirectly on claim 1. As such, claims 2-4 and 6-9 are patentable for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

2. Rejection of Claims 1-4, 6-11, and 14-25 Under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1-4, 6-11, and 14-25 under 35 U.S.C. §103(a) as being unpatentable over Robbins et al. (J. Clin. Microbiol. 1987) and Lambert (J. Applied Microbiol.) in view of Syverson (U.S. 5,612,045) or Syverson in view of Robbins et al. and Lambert.

Claim 1 is discussed above.

Robbins et al. and Lambert are discussed above. As discussed above, neither Robbins et al. nor Lambert teach or suggest the use of a first active ingredient having the structure as required in claim 1 on a non-absorbent substrate, selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche, for insertion into the vagina for inhibiting exoproteins from Gram positive bacteria. The Syverson reference does not overcome this deficiency. Specifically, Syverson is merely directed to absorbent articles,

such as catamenial tampons, which include an effective amount of an ether compound to substantially inhibit the production of exotoxins by Gram positive bacteria. Significantly, nowhere in Syverson is a first active ingredient as set forth in claim 1 even mentioned, much less that such a compound has antimicrobial properties or is effective in inhibiting the production of exoprotein from Gram positive bacteria when deposited on a non-absorbent substrate selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.

As none of the cited references teach or suggest using the first active ingredient having the structure as set forth in claim 1 on a non-absorbent substrate, selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche, for insertion into the vagina for inhibiting exoproteins from Gram positive bacteria, claim 1 is patentable over the combination of Robbins et al., Lambert, and Syverson.

3. Rejection of Claims 1-4, 6-11, and 14-25 Under Non-Statutory Obviousness-type Double Patenting

Claims 1-4, 6-11, and 14-25 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-6, 10-11, 16-31, 34-46, and 48-51 of copending Application No. 09/969,299 in view of Robbins et al.

Applicants note this rejection is in fact a provisional obviousness-type double patenting rejection since U.S. Patent

Application No. 09/969,299 has not yet issued as a patent. Applicants will address the merits of these rejections, as appropriate, if the listed application issues as a patent before the application at hand.

Conclusion

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee deficiency in connection with this Letter To Patent And Trademark Office to Deposit Account Number 01-2384.

Respectfully Submitted,

/Christopher M. Goff/

Christopher M. Goff, Reg. No. 41,785
ARMSTRONG TEASDALE LLP
One Metropolitan Square, 26th Floor
St. Louis, Missouri 63102
314-621-5070

CMG/JMB/dhm
Via EFS